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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	08

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/616,849	Applicant(s) BURCHARD, JULJA	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-75 and 81-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-75 and 81-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to papers filed 5 February 2002 in Paper No. 7 in which claims 1, 4-13, 15, 20, 22, 23, 25, 27-30, 33-40, 42-47, 55-59, 62, 67-72, 75 and 85 were amended and claims 2, 3, 31, 32 and 41were canceled. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 6 dated 5 November 2001 under 35 U.S.C. 112, second paragraph § a, b, e, h, w, z, ee and hh are maintained. The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) are maintained. All of the arguments have been thoroughly reviewed and are discussed below.

The examiner appreciates Exhibits B and C: Pending Claims. A complete set of pending claims facilitates examination.

The examiner's Art Unit has changed from 1655 to 1634. Please address future correspondence to Art Unit 1634.

Currently claims 1, 4-30, 33-40, 42-75 and 81-85 are under prosecution.

Specification

2. The previous objection to the specification is withdrawn in view of Applicant's amendments of Paper No. 7.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 3-30, 33-40, 42-75 and 81-85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1, 3-30, 33-40, 42-75 and 81-85 are indefinite as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are the method steps for comparing the amount of binding to thereby evaluate binding of probe to target. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter the claims encompass as well as make clear the subject matter from which others would be precluded. *Ex parte Erlich*, 3 USPQ2d 1011 at 6. It is suggested that Claims 1, 27 and 67 be amended to recite the essential steps for determining sensitivity e.g. hybridizing, measuring, determining.

b. Claims 1, 3-30, 33-40, 42-75 and 81-85 are indefinite for recitation of the term "pure" because "pure" is non-specific relative term which require definition or criteria for determining. Because "pure" is a non-specific term, one of skill in the art would not be appraised of the scope of the claim. It is suggested that the claims be amended to define or recite criteria for determining "pure".

e. Claims 8 and 9 are further indefinite in Claim 8 for the recitation "sensitivity of the probe" because essential steps for determining "sensitivity" are omitted, such omission amounting to a gap between the steps. See MPEP § 2172.01. It is suggested that Claim 8 be amended to recite the essential steps for determining sensitivity e.g. hybridizing, measuring, determining.

h. Claims 10 and 11 are further indefinite in Claim 10 for the recitation "specificity of the probe" because essential steps for determining "specificity" are omitted, such omission amounting to a gap between the steps. See MPEP § 2172.01. It is suggested that Claim 10 be

amended to recite the essential steps for determining sensitivity e.g. hybridizing, measuring, comparing, determining.

w. Claims 55 and 56 are further indefinite in Claim 55 for the recitation "sensitivity of the probe" because essential steps for determining "sensitivity" are omitted, such omission amounting to a gap between the steps. See MPEP § 2172.01. It is suggested that Claim 55 be amended to recite the essential steps for determining sensitivity e.g. hybridizing, measuring, determining.

z. Claims 57 and 58 are further indefinite in Claim 57 for the recitation "specificity of the probe" because essential steps for determining "specificity" are omitted, such omission amounting to a gap between the steps. See MPEP § 2172.01. It is suggested that Claim 57 be amended to recite the essential steps for determining sensitivity e.g. hybridizing, measuring, comparing, determining.

ee. Claims 69 and 70 are further indefinite in Claim 69 for the recitation "sensitivity of the probe" because essential steps for determining "sensitivity" are omitted, such omission amounting to a gap between the steps. See MPEP § 2172.01. It is suggested that Claim 69 be amended to recite the essential steps for determining sensitivity e.g. hybridizing, measuring, determining.

hh. Claims 71 and 72 are further indefinite in Claim 71 for the recitation "specificity of the probe" because essential steps for determining "specificity" are omitted, such omission amounting to a gap between the steps. See MPEP § 2172.01. It is suggested that Claim 71 be amended to recite the essential steps for determining sensitivity e.g. hybridizing, measuring, comparing, determining.

Response to Arguments

5. Applicant argues regarding § a above that the method step of comparing is the only essential step and therefore other method steps e.g. labeling, hybridizing, detecting, measuring, and comparing are not essential. The argument has been considered but is not found persuasive because the claims are drawn to a method for evaluating binding properties but the claims do not recite method steps for evaluating binding properties. Independent claims 1, 27

and 67 recite a method step of comparing amount of binding of molecules, but the claims do not recite a single method step of binding evaluation. Therefore, the claims are indefinite for omitting essential steps of binding evaluation.

Applicant argues regarding § e, w and ee above that the only essential method step for determining sensitivity is determining the absolute amount of binding and other steps are not essential to the claimed method. The argument has been considered but is not found persuasive because the claims do not recite method steps for determining absolute amount and they do not define how the absolute amount determines specificity. Therefore, the claims are indefinite for omitting essential steps.

Applicant argues regarding § h, z and hh above that the only essential method step for determining specificity is determining the absolute amount of binding and other steps are not essential to the claimed method. The argument has been considered but is not found persuasive because the claims do not recite method steps for determining absolute amount and they do not define how the absolute amount determines specificity. Therefore, the claims are indefinite for omitting essential steps.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 3-30, 33-36, 38-40, 43-45, 48-75 and 81-85 are rejected under 35 U.S.C. 102(b) as being anticipated by Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998).

Regarding Claims 1, 27 and 67, Brown et al. disclose methods for evaluating binding of a plurality of polynucleotide probes to a target polynucleotide wherein each probe has a particular nucleotide sequence, said method comprising comparing the amount of

hybridization in a first sample to the amount of hybridization in a second sample and wherein the first sample comprises a plurality of the same target polynucleotides (i.e. amplified copies of fragments from the large chromosomes) and the second sample comprises a plurality of different polynucleotide molecules wherein the different polynucleotide molecules have a different nucleotide sequence (i.e. the second sample comprises amplified copies of fragments from the small chromosomes) (Example 1, Column 16, line 39-56) wherein the first sample is at least 75% pure in said target molecule.

The claims are given the broadest reasonable interpretation consistent with the indefinite claim language. The chromosome target molecules of Brown et al. are reasonably interpreted as "75% pure" because the chromosomes are gel extracted and then amplified. Therefore the chromosome target molecules are reasonably interpreted as at least 75% pure in target molecule. Additionally, Brown et al teach an embodiment wherein each probe has a particular nucleotide sequence, said method comprising comparing the amount of hybridization in a first sample to the amount of hybridization in a second sample and wherein the first sample comprises a plurality of the same target polynucleotides (i.e. cDNAs produced from mRNAs extracted from wild-type Arabidopsis) and the second sample comprises a plurality of different polynucleotide molecules (i.e. cDNAs produced from mRNAs extracted from transgenic Arabidopsis) wherein the different polynucleotide molecules have a different nucleotide sequence and wherein the first samples is at least 75% pure target molecule (Column 17, line 42-Column 18, line 30). As stated above, the claims are indefinite because "pure" is a non-specific relative term. The cDNA target molecules of Brown et al are reasonably interpreted as being at least 75% pure because the mRNAs are isolated from the cell and then reverse transcribed to provide cDNA target molecules (Column 17, lines 56-60). Therefore, the cDNA target molecules are at least 75% pure target molecules.

Regarding Claims 4-6 and 33-35, Brown et al. disclose the methods wherein the first sample is at least 99% pure target because the chromosome target molecules are gel-extracted

and amplified (Column 16, lines 39-47) and because the mRNAs are isolated from the cell and then reverse transcribed to provide cDNA target molecules (Column 17, lines 56-60). . As stated above, the claims are indefinite because "pure" is a non-specific relative term. The claims are given the broadest reasonable interpretation consistent with the indefinite claim language. The chromosomal gel extraction/amplification and mRNA extraction/cDNA production of Brown et al. are reasonably interpreted as 90%, 95% and/or "99%" pure because they provide pure chromosomal target molecules and cDNA target molecules respectively.

Regarding Claim 7, Brown et al disclose the method wherein the plurality of different molecules in the second sample is different form the target molecules in the first sample i.e. (Example 1: the first sample comprises the largest chromosomes and the second sample comprises the smallest chromosomes (Column 16,lines 42-43) and in Example 2:, the first sample comprises cDNAs from wild-type Arabidopsis and the second sample comprises transgenic Arabidopsis (Column 17, lines 65-60).

Regarding Claim 8, 55 and 69, Brown et al. disclose the method wherein the sensitivity of the probe is determined (Column 16, line 66-Column 17, line 8). As stated above, the claim is indefinite because it is unclear how the sensitivity is determined. However, Brown et al. determine amount of binding which, according to the specification, determines sensitivity (Column 16, line 66-Column 17, line 8). Therefore, Brown et al. disclose the claimed method.

Regarding Claim 9, 56 and 70, Brown et al. disclose the method wherein the sensitivity is determined from the amount of binding to the target in the first sample to the probe (Column 16, line 66-Column 17, line 8).

Regarding Claim 10, 57 and 71, Brown et al. disclose the method wherein the specificity of the probe is determined (Column 17, lines 9-17). As stated above, the claim is indefinite because it is unclear how the specificity is determined. However, Brown et al. determines the amount of hybridization vs. non-specific hybridization by determining the amount of

chromosome-specific vs. non-specific binding (Column 17, lines 9-17). Therefore, Brown et al. disclose the claimed method.

Regarding Claim 11, 58 and 72, Brown et al. disclose the method wherein the specificity is determined by the ratio of specific to non-specific binding (Column 17, lines 9-17).

Regarding Claims 12 and 59, Brown et al. disclose the method wherein the target polynucleotide molecules in the first sample are detectably labeled (Column 16, lines 47-54).

Regarding Claims 13 and 60, Brown et al. disclose the method wherein the polynucleotide molecules in the second sample are detectably labeled (Column 16, lines 47-54).

Regarding Claims 14 and 61, Brown et al. disclose the methods of 12, 13, 59 and 60 wherein the polynucleotides are labeled with a fluorescent molecule (Column 16, lines 47-54).

Regarding Claims 15 and 62, Brown et al. disclose the method wherein the polynucleotides in the first sample are labeled with a first label and the polynucleotides in the second sample are labeled with a second label distinguishable from the first label (Column 16, lines 47-54).

Regarding Claims 16 and 63, Brown et al. disclose the method wherein the first and second labels are fluorescent molecules (Column 16, lines 47-54).

Regarding Claims 17, 64 and 73, Brown et al. disclose the method wherein each of the plurality of polynucleotide probes is attached to a surface of a support (Column 16, lines 23-30).

Regarding Claims 18 and 65, Brown et al. disclose the method wherein the probe is one of a plurality of probes (Column 16, lines 23-30).

Regarding Claims 19, 26, 66 and 74, Brown et al. disclose the method wherein the plurality of probes comprises probes in an array of probes, said array having a support with at least one surface and different probes attached to said surface and wherein each of said different probes is attached to the surface in a different location (Column 16, lines 23-30).

Regarding Claim 20, Brown et al. disclose the method wherein the probe is a polynucleotide probe having a particular nucleotide sequence (i.e. a clone sequence of *S. cervisiae* genomic DNA, Column 16, lines 10-12).

Regarding Claim 21, Brown et al. disclose the method wherein the molecules of the target molecule in the first sample are polynucleotide molecules (Column 16, lines 45-56).

Regarding Claims 22, 28 and 68 Brown et al. disclose the method wherein the probe is complementary to at least a portion of the polynucleotide molecules in the first sample (Column 17, lines 9-17 and Fig 6).

Regarding Claim 23, Brown et al. disclose the method wherein the different target molecules in the second sample have sequence that is different from the polynucleotides in the first sample (Column 17, lines 9-17 and Fig 6).

Regarding Claim 24, Brown et al. disclose the method wherein the probe is attached to a surface of a support i.e. produce a green signal (Column 17, lines 46-50).

Regarding Claim 25, Brown et al. disclose the method wherein the probe is one of a plurality of probes having different nucleotide sequences (i.e. a clone sequence of *S. cervisiae* genomic DNA, Column 16, lines 10-12).

Regarding Claim 29, Brown et al. disclose the method wherein the target polynucleotide in the first sample corresponds to a gene or gene transcript i.e. the target is from a chromosome which contains genes and therefore the target "corresponds" to a gene (Column 16, lines 39-45).

Regarding Claim 30, Brown et al. disclose the method wherein the different polynucleotide molecules in the second sample corresponds to a plurality of different genes i.e. the polynucleotides in the second sample are from different chromosomes and chromosomes contain genes therefore, second sample "corresponds" to different genes (Column 16, lines 39-45).

Regarding Claim 36, Brown et al. disclose the method wherein each different polynucleotide in the second sample has a nucleotide sequence different from the target sequence i.e. the different polynucleotide sequences in the second sample have a sequence different form the target molecule as illustrated by the small chromosome-specific green signal (Column 17, lines 12-14).

Regarding Claim 38, Brown et al. disclose the method wherein the polynucleotides in the second sample comprises polynucleotides having the same sequence as polynucleotides in the first sample and a plurality of different polynucleotides i.e. the different polynucleotides produce a green signal and the polynucleotides having the same sequence produce an orange signal (Column 17, lines 9-17).

Regarding Claim 39, Brown et al. disclose the method wherein the target polynucleotide corresponds to a gene i.e. the target is from a chromosome which contains genes and therefore the target "corresponds" to a gene (Column 16, lines 39-45) and the second sample comprises a polynucleotide sample from a wild-type strain of the cell wherein the wild-type expresses the gene corresponding to the target polynucleotide i.e. the first and second sample are from the wild-type *S. cervisiae* which expresses the gene "corresponding" to the target molecule within the six largest chromosome (Column 16, lines 39-56).

Regarding Claim 40, Brown et al. disclose the method wherein the first sample comprises polynucleotide molecules having a sequence different from the target polynucleotide (i.e. the sample has more than one different polynucleotides of different sequence) and the second sample lacks the different polynucleotides i.e. the red fluorescent signal identifies polynucleotides in the first sample lacking in the second sample (Column 17, lines 9-17).

Regarding Claim 43, Brown et al. disclose a method wherein the first sample comprises polynucleotide molecules having a sequence different from the target polynucleotide (i.e. the sample has more than one different polynucleotide of different sequence) and the second sample comprises polynucleotides having the same sequence as the target and a plurality of

different polynucleotides i.e. the green fluorescent signal identifies polynucleotides in the first sample lacking in the second sample, the red fluorescent signal identifies polynucleotides different from the first sample and yellow fluorescent signal identifies polynucleotides common between the samples (Column 18, lines 5-17).

Regarding Claim 44, Brown et al. disclose the method wherein the amount of target molecule in the first sample differs from the amount in the second sample by at least a factor of four (Column 17, lines 51-55).

Regarding Claim 45, Brown et al. disclose the method wherein the amount of target molecule in the first sample differs from the amount in the second sample by at least a factor of eight (Column 17, lines 51-55).

Regarding Claim 48-54, Brown et al. disclose the method wherein the amount of the polynucleotides in the first and second sample differ by no more than a factor of 100 (Claim 48); differ by no more than a factor of 10 (Claim 49); differ by no more than 50% (Claim 50); differ by no more than a factor of two (Claim 51); and the abundances differ no more than 50% (Claim 52); by nor more than 10% (Claim 53); and differ by no more than 1% (Claim 54); i.e. the amount and abundance are the same (Column 17, lines 65-67).

Regarding Claim 75, Brown et al. disclose the method of Claim 67 wherein the first sample comprises two or more different polynucleotides and wherein the none of the different polynucleotides hybridizes or cross-hybridizes to a probe that also hybridizes to another of the different polynucleotides i.e. hybridization conditions are used that result in hybridization of complementary polynucleotides (Column 4, lines 60-64).

Regarding Claim 81, Brown et al. disclose the method of Claim 1, further comprising prior to the step of comparing, the steps of: contacting the probe with the first sample; contacting the probe with the second sample; detecting binding between the probes and molecules in the first sample; and detecting binding between the probes and the molecules in the second sample (Column 16, line 57-Column 17, line 8).

Regarding Claim 82, Brown et al. disclose the method wherein the steps of contacting are preformed concurrently (Column 17, lines 57-65).

Regarding Claim 83, Brown et al. disclose the method wherein the steps of detecting are preformed concurrently (Column 16, line 66-Column 17, line 8).

Regarding Claim 84, Brown et al. disclose the method of Claim 27 wherein polynucleotides in the first sample are labeled with a first label and polynucleotides in the second sample are labeled with a second label distinguishable from the first label and further comprising concurrently contacting the probe with the first and second sample under conditions conductive to hybridization and detecting binding that occurs between the probe and polynucleotides in the first and second sample (Column 16, line 57-Column 17, line 8).

Regarding Claim 85, Brown et al. disclose the methods of Claims 81-85 wherein the second sample lacks polynucleotides in the first sample i.e. the red fluorescent signal identifies polynucleotides in the first sample lacking in the second sample (Column 17, lines 9-17).

Response to Arguments

8. Applicant argues that the samples of Brown et al contain amplified molecules and not mostly target molecule as required by the amended claims. Applicant further argues that in Brown, both samples comprise pools of random amplification products of more than one chromosome, but Brown does not teach a sample which is at least 75% pure in target molecules or a method of evaluating binding properties of a probe to its target by comparing the binding of the probe to a sample with the binding of the probe to a sample containing different molecules. The arguments have been considered but are not found persuasive because as stated above, "pure" is a non-specific relative term. The claims recite "at least 75% (90%, 95% and 99%) pure in said target molecule", but the claims do not define a relationship in which the target molecule is 75% (90%, 95% and 99%) pure. The claims are given the broadest reasonable interpretation in view of the non-specific claim language. Given the broadest reasonable interpretation, the claimed "at least 75% (90%, 95% and 99%) pure in said target molecule" encompasses the chromosomal target molecules of Brown et al because their chromosomal target molecules are purified from the cell. Therefore, in relationship to cellular chromosomal target molecules, the chromosomal target molecules of Brown et al are at least 75% (90%, 95% and 99%) pure in target molecules. Additionally, Brown et al teach comparing

the binding of the probe to a sample (i.e. largest chromosomes) by comparing the binding of the probe to a sample comprising different molecules (i.e. smallest chromosomes) (Column 16, lines 39-56). Therefore, Brown et al disclose the claimed binding comparison.

Applicant argues that Brown et al do not teach the sensitivity of the probe that is the absolute amount of said target molecules that bind to said probe and Brown et al do not teach a sample which is at least 75% pure in a target molecule, and therefore, Brown et al do not teach the claimed method. The arguments have been considered but are not found persuasive because as stated above, the claims are given the broadest reasonable interpretation in view of the non-specific claim language. Given the broadest reasonable interpretation, the recitation "at least 75% (90%, 95% and 99%) pure in said target molecule" encompasses the chromosomal target molecules of Brown et al because their chromosomal target molecules are purified from the cell. Additionally, Brown et al teach determining sensitivity as claimed because they teach determining the absolute amount of target-to-probe binding under particular hybridization conditions (Column 4, line 60-Column 5, line 8 and Column 17, lines 1-17) as defined in the specification on page 40, lines 1-11.

Applicant argues that Brown et al do not teach determining the specificity of the probe because they do not teach specificity is the amount of said target molecules that bind to said probe relative to the amount of other molecules that bind the probe under the same conditions. The argument has been considered but is not found persuasive because Brown et al teach determining specificity because they teach determining the absolute amount of large chromosome target-to-probe binding under particular hybridization conditions by comparison to the amount of other molecules (i.e. small chromosome) under the same conditions (Column 4, line 60-Column 5, line 8 and Column 17, lines 1-17). And they specifically teach that non-specific probe binding is identified wherein both small and large chromosomes hybridize to the same probe thereby producing a yellow signal and wherein cross hybridization produces an orange signal (Column 17, lines 9-16). Finally they teach that the combination of dual-color fluorescence and control spots on the array confirm probe specificity (Column 17, lines 9-17). Therefore, Brown et al disclose the method as claimed.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 37 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998).

Regarding Claim 37, Brown et al. teach a method for evaluating binding of a plurality of polynucleotide probes to a target polynucleotide wherein each probe has a particular nucleotide sequence, said method comprising comparing the amount of hybridization in a first sample to the amount of hybridization in a second sample and wherein the first sample comprises a plurality of the same target polynucleotides (i.e. amplified copies of fragments from the large chromosomes) and the second sample comprises a plurality of different polynucleotide molecules wherein the different polynucleotide molecules have a different nucleotide sequence (i.e. the second sample comprises amplified copies of fragments from the small chromosomes) (Example 1, Column 16, line 39-56) wherein the target polynucleotide in the first sample corresponds to a gene or gene transcript i.e. the target is from a chromosome which contains genes and therefore the target "corresponds" to a gene (Column 16, lines 39-45) and they teach an embodiment of their method wherein the second sample comprises a sample from a deletion mutant wherein the deletion mutant does not express the gene (Column 15, lines 5-18). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the samples of Brown et al. to analyze samples wherein the second sample comprises a deletion mutant as they suggest to thereby rapidly evaluate probe-target binding for the expected benefit of rapid and convenient detection of mutant-specific disease state as taught by Brown et al. (Column 15, lines 59-67).

Regarding Claim 42, Brown et al. teach the method wherein the first sample comprises polynucleotide molecules having a sequence different from the target polynucleotide (i.e. the sample has more than one different polynucleotides of different sequence) and the second sample lacks the different polynucleotides i.e. the red fluorescent signal identifies polynucleotides in the first sample lacking in the second sample (Column 17, lines 9-17) wherein the target polynucleotide in the first sample corresponds to a gene or gene transcript i.e. the target is from a chromosome which contains genes and therefore the target "corresponds" to a gene (Column 16, lines 39-45) and the first sample comprises a polynucleotide sample from a wild-type strain (i.e. *S. cer*evisiae, Column 16, lines 39-41) and they teach an embodiment of their method wherein the second sample comprises a sample from a deletion mutant wherein the deletion mutant does not express the gene (Column 15, lines 5-18). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the samples of Brown et al. to analyze samples wherein the second sample comprises a deletion mutant as they suggest to thereby rapidly evaluate probe-target binding for the expected benefit of rapid and convenient detection of mutant-specific disease state as taught by Brown et al. (Column 15, lines 59-67).

Response to Arguments

11. Applicant argues that Brown et al do not teach a method of evaluating binding properties of a probe to its target by comparing binding of the probe using a sample which is at least 75% pure in target molecule and one skilled in the art would not be motivated by Brown et al to evaluate the binding properties of a probe. Applicant further argues that Brown et al does not provide an ordinary skilled person in the art a reasonable expectation of success for evaluating binding properties of a probe. The arguments have been considered but are not found persuasive because as stated above in ¶ 7 and 8, Brown et al disclose the methods as claimed.

12. Claims 46-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998) and further in view of Schena et al. (Science 1995, 270: 467-470).

Regarding Claim 46, Brown et al. teach the method wherein the first sample comprises polynucleotide molecules having a sequence different from the target polynucleotide (i.e. the sample has more than one different polynucleotide of different sequence) and the second sample comprises polynucleotides having the same sequence as the target and a plurality of different polynucleotides i.e. the green fluorescent signal identifies polynucleotides in the first sample lacking in the second sample, the red fluorescent signal identifies polynucleotides different from the first sample and yellow fluorescent signal identifies polynucleotides common between the samples (Column 18, lines 5-17) wherein the amount of target molecule in the first sample differs from the amount in the second sample by at least a factor of ten (Column 17, lines 51-55) but they do not teach the amount differs by at least a factor of 20 (Claim 46) at least factor of 100 (Claim 47). However, Schena et al. teach a similar method wherein the first sample comprises polynucleotide molecules having a sequence different from the target polynucleotide (i.e. the sample has more than one different polynucleotide of different sequence) and the second sample comprises polynucleotides having the same sequence as the target and a plurality of different polynucleotides i.e. the green fluorescent signal identifies polynucleotides in the first sample lacking in the second sample, the red fluorescent signal identifies polynucleotides different from the first sample and yellow fluorescent signal identifies polynucleotides common between the samples (page 468, right column) wherein the amount of target molecule in the first sample differs from the amount in the second sample by at least a factor of 50 (page 468, right column, first full paragraph, lines 15-22) and they teach an embodiment wherein the amount differs by at least a factor of 100 (page 469, middle column, lines 3-9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the differing amount of polynucleotides in the samples of Brown

et al. to differ by at least a factor of 100 as taught by Schena et al. and to quantitatively measure complex gene expression patterns to thereby characterize physiological and pathological conditions for the expected benefit of linking gene expression to clinical diagnosis as taught by Schena et al. (page 469, last paragraph, lines 13-24).

Response to Arguments

13. Applicant argues that Brown et al do not teach a method of evaluating binding properties of a probe to its target by comparing binding of the probe using a sample which is at least 75% pure in target molecule and one skilled in the art would not be motivated by Brown et al to evaluate the binding properties of a probe. Applicant further argues that Brown et al does not provide an ordinary skilled person in the art a reasonable expectation of success for evaluating binding properties of a probe. The arguments have been considered but are not found persuasive because as stated above in ¶ 7 and 8, Brown et al disclose the methods as claimed.

Applicant argues that Schena et al do not teach or suggest a method for evaluating the binding properties of a probe and they do not teach evaluating binding properties of a probe to its target by comparing the binding of the probe using a sample which is at least 75% pure in target molecule and therefore, Schena et al do not cure the deficiencies of Brown et al. The arguments have been considered but are not found persuasive because as stated above in ¶ 7 and 8, Brown et al disclose the claimed methods for evaluating binding properties of a probe.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
April 9, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600